

**REMARKS**

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

**I. Disposition of the Claims**

A detailed listing of all claims that are or were in the application, irrespective of whether the claims remain under examination in the application, is presented with an appropriate status identifier.

Claims 1-3, 5-7, 9-11 and 13 were pending. Of these, claims 1-3, 5-7, 10, and 11 are cancelled without prejudice or disclaimer. Claims 9 and 13 are currently amended. Claim 14 is added. Upon entry of this amendment, claims 9, 13-14 will be pending.

**II. Claim Rejections – 35 U.S.C. § 112, second paragraph**

The Office rejects claims 1, 2, 5, 6, 10, and 13 under 35. U.S.C. 112 second paragraph as being indefinite for various reasons.

First, claims 1 and 5 are rejected for allegedly presenting “self-conflicting evidence” by referring to a benzyl substituent as R1. Claims 1 and 5 are cancelled. Thus, this rejection is moot.

Second, claims 2 and 10 have been cancelled, therefore the rejection based on the use of the terms “carbocycle” and “heterocycle” is now moot.

Third, the compounds that were previously incorporated by reference in claim 13 have been clearly delineated in tabular format.

The Applicants respectfully request withdrawal of the indefiniteness rejection.

**III. Claim rejection – 35 U.S.C. § 102(b)**

The Examiner maintains a rejection of 1, 2, 8, and 9 under 35 U.S.C. 102(b) over Bycroft et al. (CA:84:106021), Gold et al. (U.S. Patent 4,818,749), and Baubbaum et al (U.S. Patent 5,319,098).

Applicants respectfully traverse the rejections of claims 1, 2, 8 and 9.

To expedite prosecution, claims 1, 2 and 8 are cancelled without prejudice to pursuing the subject matter thereof in a continuing application.

Regarding the rejection of claims 9, Applicants refer to the Office Action dated December 12, 2002 at page 4, item 3 for details on the Examiner's basis for rejection. In the third paragraph, the Examiner states that "[e]ach marked section of the reference disclosed pyruvateproline in composition with pharmaceutically acceptable organic solvent carrier, which anticipated the compositions."

Bycroft et al. discloses a compound where X is O, D is a bond, R<sup>2</sup> is cyano, and R<sup>1</sup> is methyl. This compound falls outside the scope of the instant claims because R<sup>2</sup> is not COOH and R<sup>1</sup> is not "C<sub>4</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle."

Both Burbaum et al. (U.S. Patent 5,319,098, col. 5, lines 40-60) and Gold et al. (U.S. Patent 4,818,749, col. 5, lines 9-10) disclose N-pyruvyl-L-proline in ethyl acetate and tetrahydrofuran, respectively. This compound falls outside of the scope of the instant claims because R<sup>1</sup> is methyl and thus fails to satisfy "R<sup>1</sup> is C<sub>4</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle." Therefore, the Applicants respectfully submit that claim 9 is not anticipated and request that the rejection be withdrawn.

Moreover, the present invention would not have been obvious over these references. The relevant compounds of Bycroft et al., Burbaum et al, and Gold et al., are disclosed as simple reaction intermediates. These compounds are not disclosed as pharmaceutically active. Accordingly, there would have been no suggestion to prepare a composition with

those compounds and a pharmaceutically acceptable carrier. For the purposes of chemical synthesis, the disclosed solvents would be at best reagent grade. Such reagent grade solvents would not satisfy the limitation of “pharmaceutically acceptable carrier.” There is no suggestion that pharmaceutically acceptable solvents would be desirable for the synthetic processes disclosed. Finally, there is no suggestion to replace the methyl group with “C<sub>4</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle.”

**IV. Claim Rejections – 35 U.S.C. § 112, first paragraph**

The Office rejects claims 1-2, and 9-10 for allegedly failing to comply with the written description requirement. The amendments to claim 9 render this rejection moot. Claims 1, 2 and 10 are cancelled.

**V. Claim Rejections – 35 U.S.C. § 102(e), (f), and (g)**

The Office rejects claims 1-2, 9-10 under 35 U.S.C. 102(e), (f), and (g) as being anticipated by example 2, col. 12 or claim 5, first compound of Brumby et al. U.S. Patent 6,284,779. The Office also asserts that claims 1-2, and 9-10 are anticipated by the ‘779 patent under 35 U.S.C. 102(f) and (g). The Applicants respectfully traverse.

Claims 1, 2, and 10 are cancelled. Claim 9, as amended, is clearly not anticipated by the referenced compound of the ‘779 patent. The compound of Example 2 and claim 5 of the ‘779 patent is: 3-(2-(3-pyridyl)ethyl)-5-[(2S)-1-(3,4,5-trimethoxyphenylglyoxyoyl)-pyrrolidin-2-yl]1,2,4-oxadiazole. This compound does not meet the limitations of claim 9 because, *inter alia*, R<sup>2</sup> is not -COOH. Accordingly, there is no anticipation. The Applicants respectfully request withdrawal of this rejection.

**VI. Claim Rejections – 35 U.S.C. § 103(a)**

Claims 1-3, 5-7, 9-11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamilton U.S. 5,859,031, U.S. 5,945,441, U.S. 6,177,455 and U.S. 6,291,510 (“the Hamilton patents”) in view of Silverman or Bungaard, further in view of Li et al. U.S. 5,801,187 and Li et al. U.S. 6,218,544 and Patani. The Applicants respectfully traverse.

To expedite prosecution, claims 1-3, 5-7, 10-11 are cancelled without prejudice to pursuing the subject matter thereof in a continuing application. The remaining claims at issue are claims 9 and 13.

The Hamilton patents disclose pyrrolidinyll compounds with carboxylic acid esters substituents and compositions comprising these compounds. The instantly claimed pharmaceutical compositions comprise compounds that do not require such an ester as R<sup>2</sup>. The Examiner asserts that Bungaard teaches that esters are prodrugs of carboxylic acids and that it would have been obvious to substitute the compositions of Hamilton et al., which comprise esters, with compositions comprising the instantly claimed acids. The Applicants disagree.

First, the teachings of Bungaard relate to replacement of acids with ester prodrugs. However, Bungaard does not suggest replacing active ester compounds with acids. Acids are not prodrugs of esters. Second, there is no independent teaching in the Hamilton patents or Silverman, Li, or Patani that the claimed acid-containing compositions are suitable replacements for the ester-containing compositions of Hamilton et al.

Third, there is no disclosure in the cited references suggesting that any carboxylic acids should be incorporated into pharmaceutical compositions for administration to a patient in need thereof. Given the teachings of the Hamilton patents and the unpredictable nature of the field, a skilled person would not have been motivated to make the compositions of the instant application. Accordingly, the claimed composition are, in fact, patentably distinguishable over the Hamilton compositions.

The Applicants respectfully request reconsideration and withdrawal of the rejection.

#### **VII. Obviousness-type Double Patenting Rejection**

Claims 1-3, 5-7, 9-11 and 13 are rejected for nonstatutory obviousness-type double patenting over claims 1, 4, and 18 of Hamilton U.S. 5,859,031, and claim 4 of Hamilton U.S. 6,291,510 in view of Silverman or Bungaard, further in view of Li et al. U.S. 5,801,187 and Li et al. U.S. 6,218,544 and Patani. The Applicants respectfully traverse.

To expedite prosecution, claims 1-3, 5-7, 10-11 are cancelled without prejudice to pursuing the subject matter thereof in a continuing application. The remaining claims at issue are composition claims 9 and 13. Therefore, compound claim 1 of the '031 patent and compound claim 4 of the '510 patent are no longer relevant.

The Examiner supports the rejection with the same rationale as was presented for the 103(a) rejection. The Applicants submit that the claims of the instant application are not rendered obvious over the claims 4 and 18 of the '031 patent alone or in combination with Silverman, Bungaard, Li, or Patani.

The '031 patent discloses pyrrolidinyl compounds with carboxylic acid esters as substituents and compositions comprising these compounds. The instantly claimed pharmaceutical compositions comprise compounds that do not require such an ester as R<sup>2</sup>. The Examiner asserts that Bungaard teaches that esters are prodrugs of carboxylic acids and that it would have been obvious to substitute the compositions of the '031 patent, which comprise esters, with compositions comprising the instantly claimed acids. The Applicants disagree.

First, the teachings of Bungaard relate to replacement of acids with ester prodrugs. However, Bungaard does not suggest replacing active ester compounds with acids. Acids are not prodrugs of esters. Second, there is no independent teaching in the '031 patent or Silverman, Li, or Patani that the claimed acid-containing compositions are suitable replacements for the ester-containing compositions of Hamilton et al.

Third, there is no disclosure in the cited references suggesting that any carboxylic acids should be incorporated into pharmaceutical compositions for administration to a patient in need thereof. Given the teachings of the '031 patent and the unpredictable nature of the field, a skilled person would not have been motivated to make the compositions of the instant application. Accordingly, the claimed composition are, in fact, patentably distinguishable over the Hamilton compositions.

The instant claims are not rendered obvious and the Applicants respectfully request reconsideration and withdrawal of the rejection.

**VIII. Claim Rejections – 35 U.S.C. § 102(e) or (f)**

Claims 1-3, 5-7, 9-11 and 13 have been rejected under 35 U.S.C. 102 (e) or (f) as being anticipated by US 2004/0186098 ('098 publication). Applicants respectfully traverse this rejection. Claims 1-3, 5-7, 10-11 are cancelled. Therefore, the claims at issue are claims 9 and 13.

US 2004/0186098 claims priority to U.S. Application No. 09/159,105 filed on September 23, 1998, U.S. Provisional Application No. 60/059,963 filed on September 25, 1997, and U.S. Provisional Application No. 60/059,905 filed on September 24, 1997. The Examiner cites pages 62-66 of the '098 publication as anticipatory of the compounds of the instant application. The examiner relies on the U.S. provisional application numbers 60/059,905 and 60/059,963 with filing dates of September 24, 1997, and September 25, 1997, respectively, to which the '098 publication claims priority. However, the examiner does not provide any evidence that the allegedly anticipatory subject matter finds support those priority applications. Furthermore, the Examiner does not cite to any disclosure in the priority documents. Thus, the evidence and explanation fail to establish prior invention, and the rejection should be withdrawn.

Applicants have reviewed application numbers 60/059,905 and 60/059,963 and find no support for cited compounds that anticipate claims 9 and 13. Neither one of these provisional applications provides support for the subject matter relied upon by the Office for this rejection. Thus, September 23, 1998 is the earliest priority date to which the relevant subject matter of '098 publication may be entitled to claim.

This application is a divisional of U.S. Application No. 09/453,571 filed on December 2, 1999 (now US 6,331,537), which in turn is a continuation-in-part of U.S. Application No. 09/204,237 filed on December 3, 1998 (abandoned), which in turn claims the benefit of U.S. Provisional Application No. 60/087,788 filed on June 3, 1998 and U.S. Provisional Application No. 60/101,077 filed on September 18, 1998. These provisional applications provide support for the claimed subject matter that the Office contends is anticipated by the '098 publication. Since the filing dates of these provisional applications precede the '098

publication's priority date of September 23, 1998, the '098 publication is not prior art under 35 U.S.C. 102 (e) or (f).

Applicants respectfully request withdrawal of this rejection.

**IX. Conclusion**

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By 

FOLEY & LARDNER LLP  
Customer Number: 29728  
Telephone: (202) 295-4059  
Facsimile: (202) 672-5399

Rouget F. Henschel  
Attorney for Applicants  
Registration No. 39,221